

### **Amendments to the Claims**

The following listing of claims replaces all prior versions of claims in the application:

#### **Listing of Claims:**

- 1-33. (Canceled)
34. (Currently amended) A method for detecting a PXE mutation in a patient by establishing if a mutation in an MRP6 gene is associated with PXE, the method comprising ~~the steps of:~~
- a) interrogating an MRP6 nucleic acid in a patient sample for the presence of a mutation;
  - b) if present, determining if the mutation is a co-segregator with a PXE phenotype; and
  - c) identifying said patient as having a PXE mutation if a mutation is present in said MRP6 nucleic acid and the mutation is a co-segregator with said PXE phenotype.
35. (Previously presented) The method according to claim 34, wherein said patient sample is selected from the group consisting of blood, saliva, amniotic fluid, and tissue.
36. (Previously presented) The method according to claim 35, wherein the said patient sample is blood.
37. (Previously presented) The method according to claim 34, wherein said step a) comprises performing a nucleic acid sequence scanning assay.
38. (Previously presented) The method according to claim 37, wherein said scanning assay is selected from the group consisting of SSCP, DGGE, RFLP, DHPLC, and enzymatic cleavage.
39. (Previously presented) The method according to claim 34, wherein said step a) comprises a specific mutation detection assay.
40. (Previously presented) The method according to claim 39, wherein said detection assay is selected from the group consisting of oligonucleotide hybridization and primer extension assays.

41. (Previously presented) The method according to claim 34, wherein said step a) comprises a nucleic acid sequencing assay.
42. (Previously presented) The method according to claim 41, wherein said assay detects the presence of a mutation selected from the group consisting of a deletion, a substitution, an insertion, and a rearrangement.
43. (Previously presented) The method according to claim 34, wherein said mutation is a non-conserved amino acid substitution.
44. (Previously presented) The method according to claim 34, wherein said mutation is in a splice site in an intron.
45. (Previously presented) The method according to claim 34, wherein said mutation is in the promoter region of the MRP6 gene.
46. (Previously presented) The method according to claim 34, wherein said mutation is in a polyA site of the MRP6 gene.
47. (Previously presented) The method according to claim 34, wherein said mutation is in an exon of the MRP6 gene.
48. (Previously presented) The method according to claim 47, wherein said exon is selected from exons 1-31 of the MRP6 gene.
49. (Previously presented) The method according to claim 34, wherein said nucleic acid is selected from the group consisting of mRNA, genomic DNA, and cDNA.
50. (Previously presented) The method according to claim 34, wherein said step a) comprises a hybridization assay.
51. (Previously presented) The method according to claim 34, wherein said step b) comprises screening the mutation against a control panel of MRP6 genes isolated from normal individuals.
52. (Previously presented) The method according to claim 34, wherein said step b) comprises comparing the mutation with a list of known PXE mutations.

53. (Previously presented) The method according to claim 34, wherein the said PXE phenotype comprises a skin manifestation.
54. (Previously presented) The method according to claim 53, wherein the said skin manifestation comprises a skin lesion found in at least one of the areas in the group consisting of face, neck, axilla, antecubital fossa, popliteal fossa, groin and periumbilical.
55. (Previously presented) The method according to claim 53, wherein the said skin manifestation comprises a laxity and a loss of elasticity of the skin found in at least one of the areas in the group consisting of face, neck, axilla, antecubital fossa, popliteal fossa, groin and periumbilical.
56. (Previously presented) The method according to claim 53, wherein the said skin manifestation comprises the calcification of fragmented elastic fibers in the mid- and lower dermis.
57. (Previously presented) The method according to claim 34, wherein said PXE phenotype is an ocular manifestation.
58. (Previously presented) The method according to claim 57, wherein said ocular manifestation comprises at least one of the group consisting of retinal hemorrhage, angloid streaks, and the accumulation of abnormal elastic fibers in the Bruch's membrane.
59. (Previously presented) The method according to claim 34, wherein said PXE phenotype comprises a cardiovascular manifestation.
60. (Previously presented) The method according to claim 59, wherein said cardiovascular manifestation comprises at least one of the group consisting of premature atherosclerotic changes; intimal fibroplasia; early myocardial infarction; fibrous thickening of the endocardium; fibrous thickening of the atrioventricular valves; and atrial septal aneurysm.
61. (Previously presented) The method according to claim 34, wherein said PXE phenotype comprises gastrointestinal bleeding.

62. (Previously presented) The method according to claim 34, wherein said PXE phenotype comprises the mineralization of the elastic fibers in at least one of the group consisting of skin, arteries and retina.
63. (Currently amended) A method for screening a patient for the presence of a PXE mutation, the method comprising ~~the steps of~~:
- a) interrogating an MRP6 nucleic acid in a patient sample for the presence of a mutation known to be a co-segregator with a PXE phenotype; and
  - b) identifying said patient as having a PXE mutation if the mutation from step a) is detected in said MRP6 nucleic acid.
64. (Previously presented) The method according to claim 63, wherein said mutation is a mutation in codon 1141.
- 65-66. (Withdrawn)
67. (Currently amended) A method for identifying a patient ~~at~~ as having an increased risk of having children with PXE, the method comprising ~~the steps of~~:
- a) interrogating an MRP6 nucleic acid in a patient sample for the presence of an MRP6 allele known to be a co-segregator with a PXE phenotype; and
  - b) identifying said patient as ~~being at~~ having an increased risk of having children with PXE if the allele from step a) is detected in said-MRP6 nucleic acid.
68. (Currently amended) A method for identifying a patient ~~at~~ as having an increased risk of developing a PXE associated symptom, the method comprising ~~the steps of~~:
- a) interrogating an MRP6 nucleic acid in a patient sample for the presence of an MRP6 allele known to be a co-segregator with a PXE phenotype; and
  - b) identifying said patient as ~~being at~~ having an increased risk of developing a PXE associated symptom if the allele from step a) is detected in said MRP6 nucleic acid.
69. (Previously presented) The method according to claim 68, wherein said PXE associated symptom is cardiovascular disease.

70. (Previously presented) The method according to claim 68, wherein said PXE associated symptom is macular degeneration.

71-72. (Canceled)

73. (Previously presented) A method for testing a patient for the presence of a PXE mutation, the method comprising the steps of:

- a) interrogating a patient sample for a mutation shown to be associated with PXE, the mutation being in the MRP6 gene, and the mutation is selected from the group consisting of:
  - i) at codon 1114, nucleotide 3341G>C;
  - ii) at codon 1138, nucleotide 3413G>A;
  - iii) at codon 1141, nucleotide 3421C>T;
  - iv) at codon 1259, nucleotide 3775delT;
  - v) at codon 1298, nucleotide 3892G>T;
  - vi) at codon 1302, nucleotide 3904G>A;
  - vii) at codon 1303, nucleotide 3907G>C;
  - viii) at codon 1314, nucleotide 3940C>T; and
  - ix) at codon 1321, nucleotide 3961G>A; and
- b) identifying the patient as having a PXE mutation if the mutation from step a) is detected in the MRP6 gene.

74-78. (Withdrawn)

79. (New) A method for detecting a patient as having an increased risk of developing PXE, the method comprising:

- a) interrogating an MRP6 nucleic acid in a patient sample;
- b) determining an abnormal presence or absence of at least one nucleic acid fragment or sequence in the patient's MRP6 nucleic acid compared to a normal control; and

- c) identifying said patient as having an increased risk of developing PXE based on the determination in step b).
80. (New) A method for screening a patient for the presence of a MRP6 gene mutation, the method comprising:
- a) interrogating an MRP6 nucleic acid in a patient sample to determine an MRP6 nucleic acid sequence; and
  - b) identifying said patient as having a MRP6 gene mutation by comparing the MRP6 nucleic acid sequence from step a) to a normal MRP6 nucleic acid sequence.